

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 12 April 2000 (12.04.00)	
International application No. PCT/GB99/02731	Applicant's or agent's file reference SMW/BP5795083
International filing date (day/month/year) 20 August 1999 (20.08.99)	Priority date (day/month/year) 21 August 1998 (21.08.98)
Applicant KOUZARIDES, Tony	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

15 March 2000 (15.03.00)



in a notice effecting later election filed with the International Bureau on:

2. The election



was



was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer S. Mafla Telephone No.: (41-22) 338.83.38
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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SMW/BP5795083	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/ 02731	International filing date (day/month/year) 20/08/1999	(Earliest) Priority Date (day/month/year) 21/08/1998
Applicant CANCER RESEARCH CAMPAIGN TECHNOLOGY LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/02731

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 G01N33/68 C12Q1/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GÖRLICH D.: "Transport into and out of the nucleus" THE EMBO JOURNAL, vol. 17, no. 10, 1998, page 2721-2727 XP002123263 cited in the application the whole document	1-14
A	CHRVIA J C ET AL: "PHOSPHORYLATED CREB SPECIFICALLY TO THE NUCLEAR PROTEIN CBP" NATURE, GB, MACMILLAN JOURNALS LTD. LONDON, vol. 365, page 855-859 XP002052727 ISSN: 0028-0836 cited in the application the whole document	1-14
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☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 November 1999

Date of mailing of the international search report

03/12/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Hoekstra, S

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 99/02731

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>YANG X -J ET AL.: "A P300/CBP-ASSOCIATED FACTOR THAT COMPETES WITH THE ADENOVIRAL ONCOPROTEIN E1A" NATURE, GB, MACMILLAN JOURNALS LTD. LONDON, vol. 382, no. 8589, page 319-324 XP002050400 ISSN: 0028-0836 the whole document</p>	1-14
A	<p>ULLMAN, K.S. ET AL.: "Nuclear export receptors form Importin to exportin" CELL, vol. 90, 1 September 1997 (1997-09-01), pages 967-970, XP002123264 cited in the application the whole document</p>	1-14
A	<p>PARTHUN, M.R.: "The major cytoplasmic histone acetyltransferase in Yeast: links to chromatin replication and histone metabolism" CELL, vol. 87, 4 October 1996 (1996-10-04), page 85-94 XP002123265</p>	1-14

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 99/ 02731

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 15-23
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 15-23

Present claims 15-23 are characterised by peptides and "agents" defined by reference to a desirable characteristic or property, namely the ability to modulate interaction between Importin alpha and CREB binding protein (CBP). These claims cover all peptides and "agents" having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the claimed products by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the methods of claim 1-14.

Moreover claims 21-23 rely for their essential features on a "product-by-assay" characterisation, the assay as such having no impact on the structural features of the agents of the claims. Lacking any pointers to the structural features of the claimed agents a formulation of a meaningful search is not possible.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷: G01N 33/68, C12Q 1/48	A1	(11) International Publication Number: WO 00/11478 (43) International Publication Date: 2 March 2000 (02.03.00)
(21) International Application Number: PCT/GB99/02731 (22) International Filing Date: 20 August 1999 (20.08.99) (30) Priority Data: 9818356.9 21 August 1998 (21.08.98) GB (71) Applicant (for all designated States except US): CANCER RESEARCH CAMPAIGN TECHNOLOGY LIMITED [GB/GB]; Cambridge House, 6-10 Cambridge Terrace, Regent's Park, London NW1 4JL (GB). (72) Inventor; and (75) Inventor/Applicant (for US only): KOUZARIDES, Tony [GB/GB]; Wellcome/CRC Institute, Tennis Court Road, Cambridge CB2 1QR (GB). (74) Agents: WALTON, Seán, M. et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: ASSAYS, METHODS AND MEANS FOR MODULATING NUCLEAR LOCALISATION (57) Abstract CBP histone acetyltransferase acetylates Importin α , affecting ability of Importin α to translocate into the nucleus and import a cargo protein. Assays identify substances which modulate interaction between CBP and Importin α and acetylation of Importin α by CBP. Substances identified in the assays are useful for treatment of disorders in which Importin α plays a role.		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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EE	Estonia						

REC'D 09 JUN 2000

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference SMW/BP5795083	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) FOR FURTHER ACTION	
International application No. PCT/GB99/02731	International filing date (day/month/year) 20/08/1999	Priority date (day/month/year) 21/08/1998
International Patent Classification (IPC) or national classification and IPC G01N33/68		
Applicant CANCER RESEARCH CAMPAIGN TECHNOLOGY LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 15/03/2000	Date of completion of this report 07.06.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Weijland, A Telephone No. +49 89 2399 7490 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/02731

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-61 as originally filed

Claims, No.:

1-23 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description. pages:
☐ the claims. Nos.:
☐ the drawings. sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 15-23.

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/02731

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 15-23.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

The following document is referred to in this communication; the numbering will be adhered to the rest of the procedure:

D1: YANG X -J ET AL: 'A P300/CBP-ASSOCIATED FACTOR THAT
COMPETES WITH THE ADENOVIRAL ONCOPROTEIN E1A'
NATURE,GB,MACMILLAN JOURNALS LTD. LONDON, vol. 382, no.
8589, page 319-324

SECTION V

2. The subject matter of claims 1-14 meets the requirements of Article 33(2) PCT.

Claims 1, 2, 4, 5, 9, relating to methods comprising agents that affect the interaction between Importin α and CBP, are not disclosed in the prior art documents.

3. The subject matter of claims 1-14 meets the requirements of Article 33(3) PCT.

D1 is considered to be the closest prior art. D1 (abstract) describes the identification of p300/CBF-associated factor (P/CAF) having intrinsic histone acetylase activity. The adenoviral oncoprotein E1A disturbs the normal cellular interaction between p300/CBP and its associated histone acetylase. Claims 1, 2, 4, 5, and 9 differ **at least** from D1 in that these claims describe methods including compounds (agents) that interfere with the CBP and Importin α interactions.

The skilled person, equipped with the knowledge of D1, would have no indication to arrive at the subject matter of claims 1, 2, 4, 5 and 9, since the interaction between CBP and importin α is not suggested in the prior art documents. The present invention discloses methods including components (agents) that interfere with this interaction to influence the nuclear import mediated by importin α .

SECTION VII

4. The application should be self contained (see further Guidelines C-II 4.17) and phrases "...and incorporated by reference..." as mentioned e.g. on page 61 (line

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/02731

10-11) contravenes this requirement.